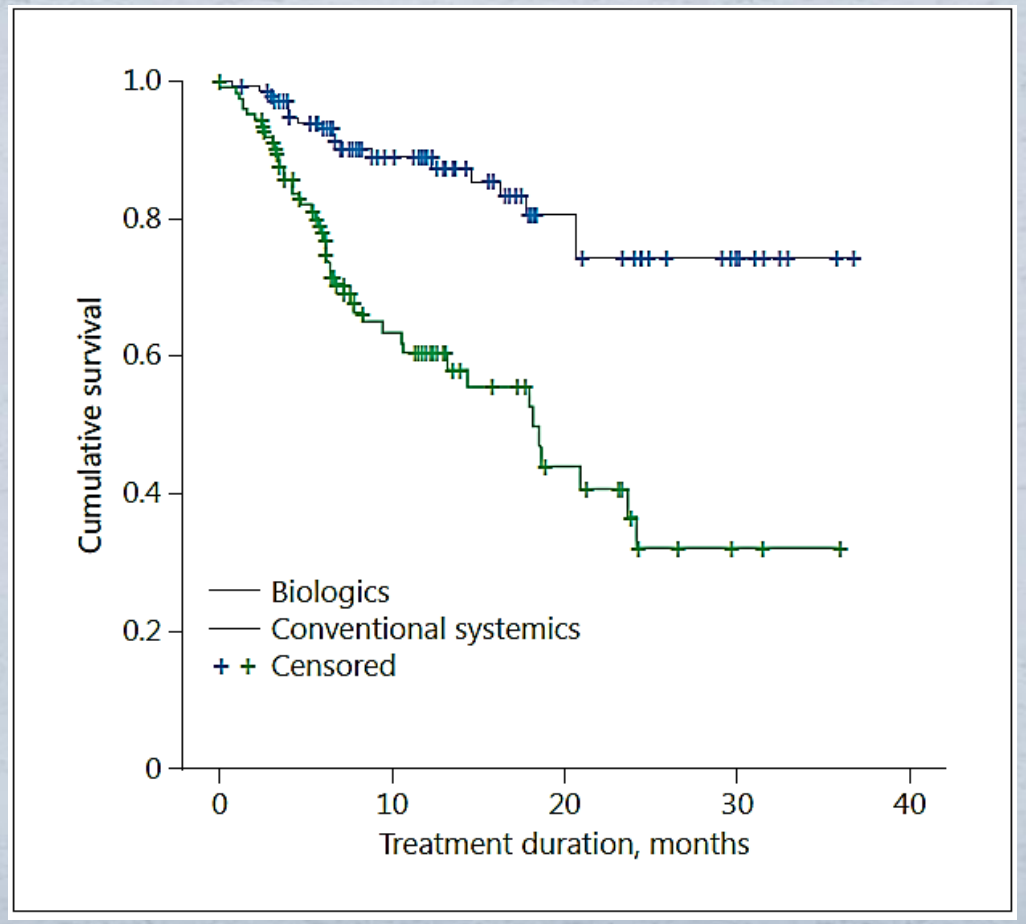
Μπορεί να συνδυαστεί η μακροχρόνια αποτελεσματικότητα με την ασφάλεια;

# Ασθενείς που παραμένουν σε θεραπεία *κλασσικές συστηματικές vs βιολογικών*

Οι ασθενείς φαίνεται να παραμένουν μεγαλύτερο χρονικό διάστημα σε θεραπεία




Efficacy and Survival of Systemic Psoriasis Treatments: An Analysis of the Swiss Registry SDNTT, Dermatology 2016;232:640–647

# Ποσοστά και λόγοι διακοπής της θεραπείας

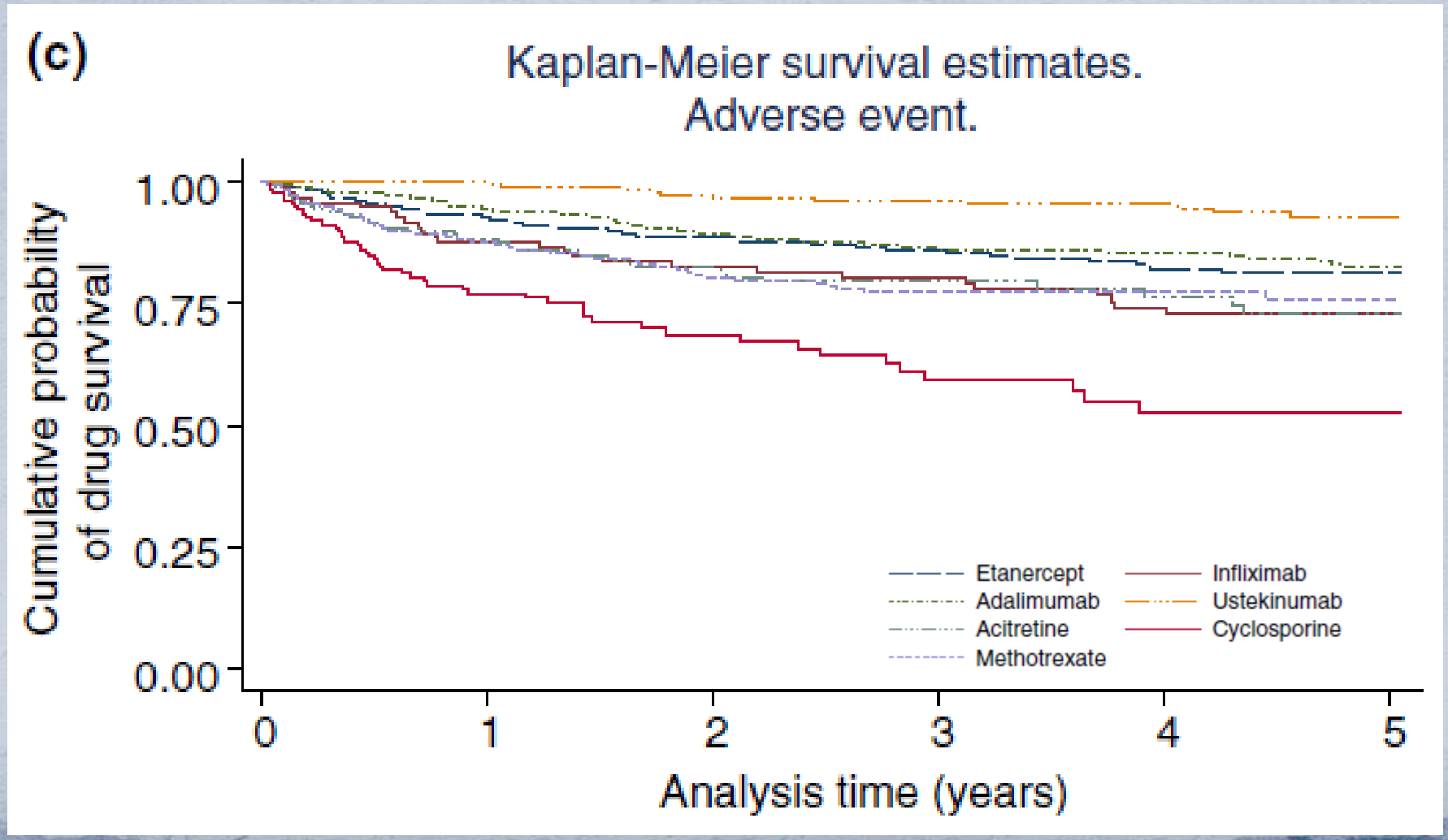
| | All | ACI | CyA | FAE | MTX | ADA | ETA | INF | UST |
|---|---|---|---|---|---|---|---|---|---|
| Treatment courses | 696 | 63 | 19 | 158 | 174 | 137 | 46 | 40 | 59 |
| Discontinued, n (%)# | 435 (62.5) | 53 (84.1) | 19 (100.0) | 108 (68.4) | 129 (74.1) | 62 (45.3) | 29 (63.0) | 26 (65.0) | 9 (15.3) |
| Adverse events, n (%)# | 210 (30.2) | 24 (38.1) | 11 (57.9) | 67 (42.4) | 69 (39.7) | 17 (12.4) | 5 (10.9) | 14 (35.0) | 3 (5.1) |
| Lack of efficacy, skin, n (%)# | 148 (21.3) | 22 (34.9) | 5 (26.3) | 33 (20.9) | 37 (21.3) | 26 (19.0) | 13 (28.3) | 8 (20.0) | 4 (6.8) |
| Lack of efficacy, joints, n (%)# | 48 (6.9) | 1 (1.6) | 0 (0.0) | 2 (1.3) | 24 (13.8) | 12 (8.8) | 7 (15.2) | 2 (5.0) | 0 (0.0) |
| Remission, n (%)# | 9 (1.3) | 2 (3.2) | 0 (0.0) | 1 (0.6) | 4 (2.3) | 1 (0.7) | 1 (2.2) | 0 (0.0) | 0 (0.0) |
| Other reason, n (%)# | 29 (4.2) | 2 (3.2) | 3 (15.8) | 9 (5.7) | 5 (2.9) | 3 (2.2) | 3 (6.5) | 3 (7.5) | 1 (1.7) |
| Not specified, n (%)# | 3 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.6) | 2 (1.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Lost to follow-up, n (%)# | 21 (3.0) | 3 (4.8) | 0 (0.0) | 5 (3.2) | 3 (1.7) | 5 (3.6) | 3 (6.5) | 1 (2.5) | 1 (1.7) |

#Due to the possibility of multiple answers, the total number of reasons given for treatment discontinuation exceeds the number of terminated treatment courses.

*Abbr.:* ACI, acitretin; ADA, adalimumab; CyA, cyclosporine A; ETA, etanercept; FAE, fumaric acid esters; INF, infliximab; MTX, methotrexate; UST, ustekinumab.

Tobias Arlond et al, Drug survival rates and reasons for drug discontinuation in psoriasis, JDDG, 1610-0379/2016/1411

# BIOBADADERM registry – Διακοπή λόγω ανεπιθύμητου συμβάντος




P. Davila-Seijo et al, Drug survival in systemic psoriasis therapy, JEADV 2016, 30, 1942–1950

# BIOBADADERM registry – Διακοπή λόγω AE στις βιολογικές θεραπείες

| | Etanercept | | Infliximab | | Adalimumab | | Ustekinumab | |
|---|---|---|---|---|---|---|---|---|
| | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation |
| **Number of AE** | 130 | 15 | 70 | 21 | 144 | 39 | 31 | 6 |
| **Number of treatments** | 736 | | 125 | | 712 | | 537 | |
| **PY** | 1229 | | 264 | | 1330 | | 1194 | |
| **Incidence *** | 10.58 (8.91-12.56) | 1.22 (0.74-2.02) | 26.52 (20.98-33.51) | 7.95 (5.19-12.20) | 10.83 (9.2-12.75)/ | 2.93 (2.14-4.01) | 2.6 (1.83-3.69)/ | 0.50 (0.23-1.12) |
| **Time to discontinuation for AE (months) Median (p25-p75)** | 16.75 (3.51-41.02)/ | 6.66 (3.21-41.01) | 8.26 (3.38-24.13) | 16.49 (3.38-24.13) | 15.69 (4.95-33.74) | 16.66 (5.38-27.44) | 12.69 (3.97-28.33) | 16.10 (1.57-40.43) |

AE adverse events, PY patient-year
*Events associated with drug discontinuation/100 PY of therapy.

J Eur Acad Dermatol Venereol. 2017 May 9. doi: 10.1111/jdv.14314. [Epub ahead of print]

# BIOBADADERM registry – Διακοπή λόγω AE στις κλασ. συστηματικές θεραπείες

| | Acitretin | | Cyclosporine | | Methotrexate | |
|---|---|---|---|---|---|---|
| | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation | **All AE** associated with drug discontinuation | **Serious AE** associated with drug discontinuation |
| **Number of AE** | 88 | 5 | 150 | 14 | 197 | 17 |
| **Number of treatments** | 555 | | 529 | | 1024 | |
| **PY** | 607 | | 305 | | 1300 | |
| **Incidence*** | 14.5 (11.76-17.87) | 0.82 (0.34-1.98) | 49.18 (41.91-57.72) | 4.59 (2.72-7.75) | 15.15 (13.18-17.42) | 1.31 (0.81-2.10) |
| **Time to discontinuation for AE (months) Median (p25-p75)** | 4.59 (1.93-14.26) | 1.87 (1.61-4.59) | 2.98 (1.15-5.67) | 5.36 (1.15-8.07) | 6.59 (2.36-17.57) | 8.07 (3.31-22.92) |

AE adverse events, PY patient-year
*Events associated with drug discontinuation/100 PY of therapy

J Eur Acad Dermatol Venereol. 2017 May 9. doi: 10.1111/jdv.14314. [Epub ahead of print]

# Ασθενείς: λόγος διακοπής της θεραπείας

| Απώλεια της αποτελεσματικότητας | Ανεπιθύμητες ενέργειες | Μη συμμόρφωση |
|---|---|---|
| Etanercept<br>Adalimumab<br>(P=0.004) | MTX (P<0.001)<br>CyA<br>Infliximab | UVB (P<0.001) |

1095 ασθενείς

| Διάμεσος χρόνος παραμονής στη θεραπεία | |
|---|---|
| Συστηματικές παραδοσιακές | 6-12 μήνες |
| Βιολογικά | 12-20.5 μήνες |

**Yeung** H, et al. J Am Acad Dermatol. **2013** Jan;68(1):64-72.

# Κλασσικές Συστηματικές Θεραπείες

Επίτευξη **PASI 75**

- **Μεθοτρεξάτη** (MTX): **24–65%**
- **Κυκλοσπορίνη** (CsA): **75–89%** (υψηλή δόση)
- **Ασιτρετίνη**: **23%**

**Η μακροχρόνια χορήγηση** τους μπορεί να **περιορίζεται λόγω ανεπιθύμητων ενεργειών** και απαιτείται τακτική και στενή παρακολούθηση των ασθενών.

ειδικότερα…

# CyA σε συνεχή χορήγηση

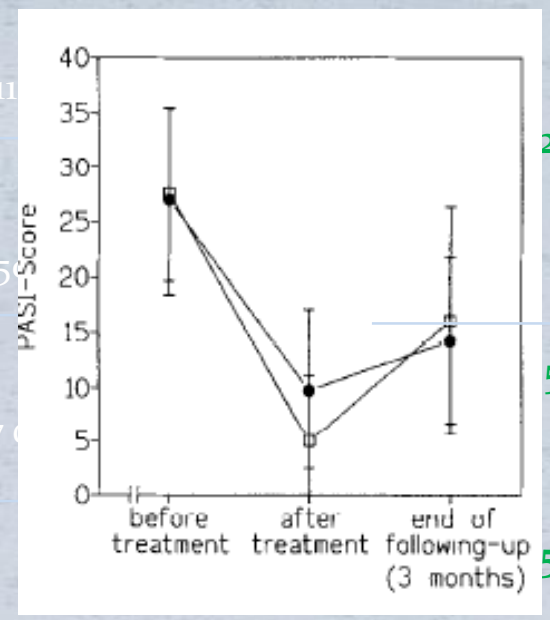
**W12**

285 ασθενείς

1.25mg/kg

2.5mg/kg

5mg/kg




**W130**

**5 ασθενείς**
**PASI=3.5**

**88 PASI 75**

**24 αποσύρθηκαν**

- Η CyA είναι αποτελεσματικό φάρμακο στη διατήρηση μιας καλής κλινικής ανταπόκρισης, αλλά εγείρονται θέματα ασφάλειας με προέχουσα τη νεφρική βλάβη (σωληναριακή ατροφία, αρτηριακή υαλινοποίηση, σπειραματική ίνωση).

Mrowietz U et al. J Am Acad Dermatol. 1995 Sep;33(3):470-5.

# Κυκλοσπορίνη (CyA): μακροχρόνια χορήγηση & αποτελεσματικότητα

JEADV

OCTOBER 2009, VOLUME 23, SUPPLEMENT 2

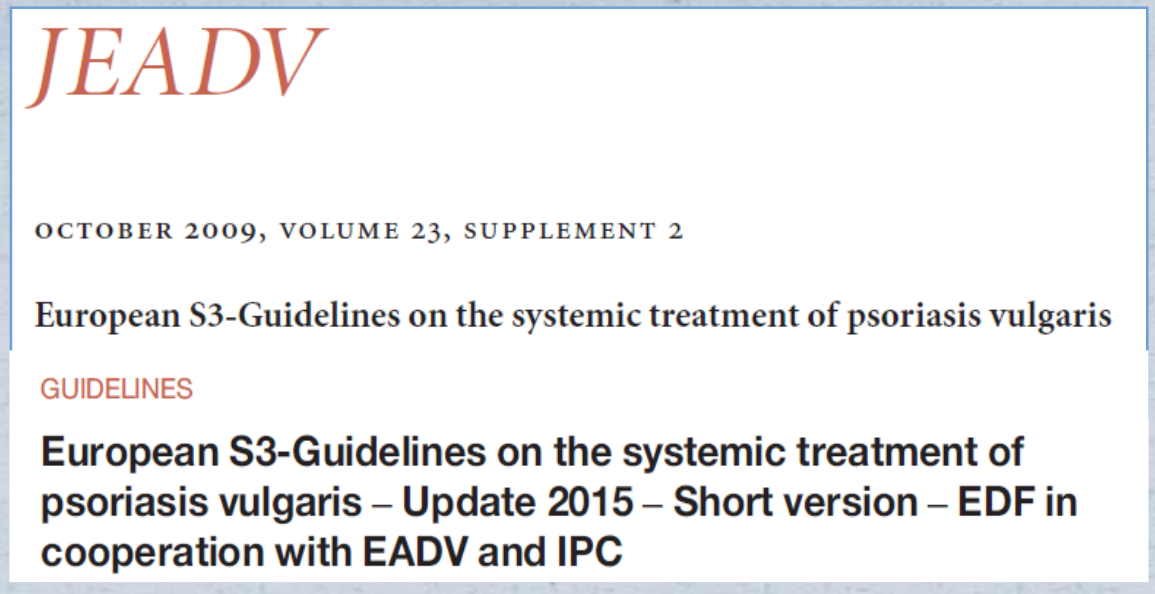
European S3-Guidelines on the systemic treatment of psoriasis vulgaris

GUIDELINES

**European S3-Guidelines on the systemic treatment of psoriasis vulgaris – Update 2015 – Short version – EDF in cooperation with EADV and IPC**

Η μακροχρόνια χορήγηση της CyA (<2 έτη) θα πρέπει να είναι η εξαίρεση, παρά ο κανόνας

# **Μεθοτρεξάτη**: μακροχρόνια χορήγηση & αποτελεσματικότητα

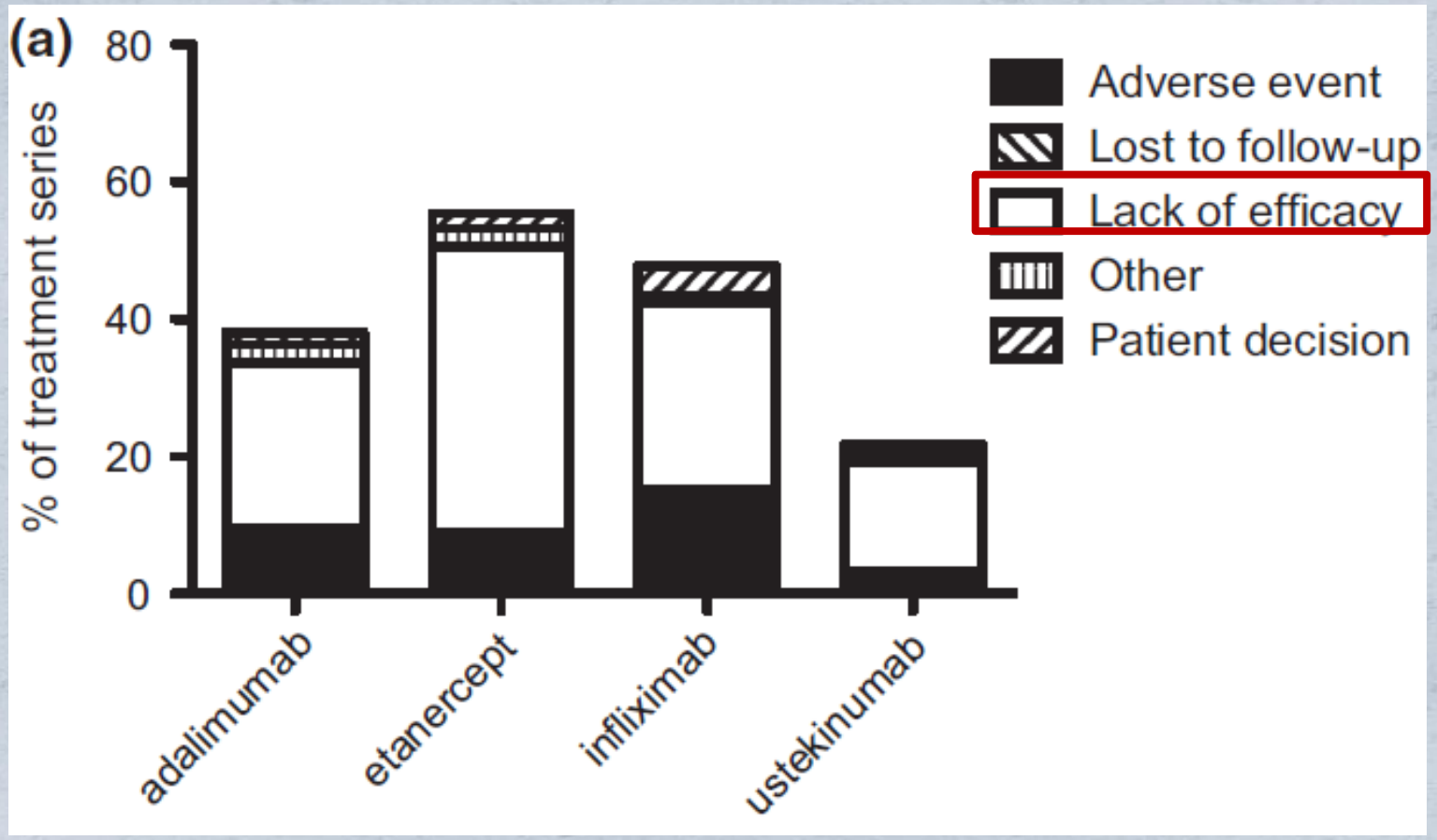



- Η κλινική εμπειρία με τη MTX είναι υψηλότερη απ΄ότι η τεκμηριωμένη στις κλινικές μελέτες.
- Η αποτελεσματικότητα του φαρμάκου αυξάνεται με το χρόνο & μπορεί να αποτελεί επιλογή μακροχρόνιας θεραπείας.

Η χρήση της περιορίζεται κυρίως από τον κίνδυνο αλληλεπιδράσεων με άλλα φάρμακα, της ηπατοτοξικότητας, της μυελικής καταστολής, των πεπτικών ελκών κ.α.

Τι συμβαίνει με τις βιολογικές θεραπείες;

# Βασικός λόγος διακοπής της βιολογικής θεραπείας η απώλεια της αποτελεσματικότητας




Biologic survival in psoriasis R. Gniadecki et al, British Journal of Dermatology (2015) 172, pp244–252

# Five-year analysis from the ESPRIT 10-year postmarketing surveillance registry of adalimumab treatment for moderate to severe psoriasis

Alan Menter, MD,[a] Diamant Thaçi, MD,[b] Kim A. Papp, MD,[c] Jashin J. Wu, MD,[d] Mareike Bereswill, MS,[e] Henrique D. Teixeira, PhD,[f] Simone Rubant, PhD,[e] and David A. Williams, MD[f]
*Dallas, Texas; Lübeck and Ludwigshafen, Germany; Waterloo, Ontario, Canada; Los Angeles, California; and North Chicago, Illinois*

***Background:*** ESPRIT is an ongoing, 10-year, observational registry, evaluating long-term safety and effectiveness of adalimumab treatment in routine clinical practice for patients with moderate to severe, chronic plaque psoriasis.

***Objectives:*** Initial 5-year results are reported.

***Methods:*** Two populations were analyzed: the "all-treated" population received 1 or more adalimumab doses in registry, continuing adalimumab treatment from a current prescription or previous study participation, and included the "new-prescription" population initiating adalimumab 4 weeks or earlier preregistry entry.

***Results:*** Data were collected from September 26, 2008, through November 30, 2013, for all-treated (n = 6059), which included new-prescription (n = 2580, 42.6%); median registry exposure was 765 and 677 days, respectively. In all-treated, rate (events per 100 patient-years of total adalimumab exposure [E/100PY]) of serious treatment-emergent adverse events (inside or outside of the registry) was 4.3 E/100PY, serious infection 1.0 E/100PY, malignancies 0.9 E/100PY (nonmelanoma skin cancers 0.6 E/100PY; melanomas <0.1 E/100PY). Standardized mortality ratio was 0.30 (95% confidence interval 0.19-0.44). Physician Global Assessment clear or minimal (effectiveness parameter) was achieved by 57.0% at 12 months and 64.7% at 60 months of treatment.

***Limitations:*** Observational data are subject to outcome-reporting bias.

***Conclusion:*** No new safety signals were observed with adalimumab treatment during this initial 5-year registry review. Observed number of deaths was below expected. As-observed effectiveness remained stable through 60 months. (J Am Acad Dermatol 2015;73:410-9.)

ORIGINAL RESEARCH ARTICLE

Am J Clin Dermatol 2011; 12 (5): 321-337
1175-0561/11/0005-0321/$49.95/0


# The Long-Term Safety of Adalimumab Treatment in Moderate to Severe Psoriasis

## A Comprehensive Analysis of All Adalimumab Exposure in All Clinical Trials

*Craig Leonardi,*[1] *Kim Papp,*[2] *Bruce Strober,*[3] *Kristian Reich,*[4] *Akihiko Asahina,*[5] *Yihua Gu,*[6] *Joseph Beason,*[6] *Stephen Rozzo*[6] and *Stephen Tyring*[7]

1 Central Dermatology, St. Louis, MO, USA
2 Probity Medical Research, University of Western Ontario, Waterloo, ON, Canada
3 Department of Dermatology, New York University School of Medicine, New York, NY, USA
4 Dermatologikum Hamburg, Hamburg, Germany
5 Sagamihara National Hospital, Sagamihara, Japan
6 Abbott Laboratories, Abbott Park, IL, USA
7 University of Texas Health Science Center, Department of Dermatology, Center for Clinical Studies, Houston, TX, USA

## Abstract

**Background:** A favorable benefit-risk profile has been established for adalimumab, with up to 5 years of treatment in 13 clinical trials in patients with moderate to severe chronic plaque psoriasis.
**Objective:** The aim of this analysis was to assess the long-term safety of all adalimumab exposure in all psoriasis clinical trials.
**Methods:** A total of six sets of data were analyzed as follows: (i) all cumulative safety data from all exposure for all adalimumab-treated patients in the 13 clinical trials in moderate to severe psoriasis (All Adalimumab Treatment Population) through April 2007, November 2008, and November 2009, respectively; (ii) longitudinal data for 1403 patients treated with adalimumab 40 mg every other week (eow) dosing (Every Other Week Population) through June 2007 and April 2010; and (iii) data from placebo-controlled periods of clinical trials. Adverse events that occurred up to 70 days after the final dose of adalimumab were analyzed.
**Results:** During placebo-controlled periods, a total of 572 patients had 173.0 patient-years (PYs) of exposure to placebo and 1188 patients had 370.5 PYs of exposure to adalimumab. Adverse event incidence rates, expressed as events per 100 PYs (events/100 PYs), for placebo- and adalimumab-treated patients for serious adverse events were 7.52 and 8.64, and for serious infectious adverse events were 2.89 and 2.43, respectively.
In the 2007, 2008, and 2009 All Adalimumab Treatment Population there were, respectively, 1819 patients (2424.7 PYs), 2197 patients (4351.9 PYs), and 3010 patients (4844.7 PYs), with serious adverse event incidence rates of 6.51, 7.22, and 8.36 events/100 PYs, and serious infectious adverse event rates of 1.32, 1.38, and 1.65 events/100 PYs.
In the 2007 and 2010 Every Other Week Population (n = 1403), there were 1883.5 and 2854.1 total PYs of exposure, respectively, with serious adverse event incidence rates of 6.32 and 6.87 events/100 PYs, and serious infectious adverse event rates of 1.33 and 1.37 events/100 PYs, respectively.
**Conclusions:** Multiple lines of evidence from a total of six sets of safety data, with treatment for up to 5 years, including results from all adalimumab-treated patients, and a subset of patients treated with 40 mg eow dosing, did not show evidence of cumulative toxicity, and showed adverse event rates that were generally stable or decreased with increased mean per-patient exposure.

# The Long-Term Safety of Adalimumab Treatment in Moderate to Severe Psoriasis

## A Comprehensive Analysis of All Adalimumab Exposure in All Clinical Trials

*Craig Leonardi,*[1] *Kim Papp,*[2] *Bruce Strober,*[3] *Kristian Reich,*[4] *Akihiko Asahina,*[5] *Yihua Gu,*[6] *Joseph Beason,*[6] *Stephen Rozzo*[6] and *Stephen Tyring*[7]

J Dermatolog Treat. 2015;26(6):493-501. doi: 10.3109/09546634.2015.1027167. Epub 2015 Apr 17.

**Evidence-based adverse effects of biologic agents in the treatment of moderate-to-severe psoriasis: Providing clarity to an opaque topic.**

Sorenson E[1], Koo J[2].

## Ψωρίαση και ασφάλεια

- Οι βιολογικοί παράγοντες είναι σχετικά ασφαλή φάρμακα
- Ανεπιθύμητες ενέργειες που έχουν αναφερθεί σε στατιστικά σημαντικό βαθμό στις διάφορες δημοσιευμένες μελέτες αφορούν σε:
  - Ελαφρά αύξηση των NMSC
  - Ελαφρά αύξηση των αιματολογικών κακοηθειών
  - Αντιδράσεις στο σημείο έγχυσης
  - Κεφαλαλγία
  - Λοιμώξεις του ανώτερου αναπνευστικού

# Ποσοστά και λόγοι διακοπής της θεραπείας

| | All | ACI | CyA | FAE | MTX | ADA | ETA | INF | UST |
|---|---|---|---|---|---|---|---|---|---|
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| Lack of efficacy, skin, n (%)# | 148 (21.3) | 22 (34.9) | 5 (26.3) | 33 (20.9) | 37 (21.3) | 26 (19.0) | 13 (28.3) | 8 (20.0) | 4 (6.8) |
| Lack of efficacy, joints, n (%)# | 48 (6.9) | 1 (1.6) | 0 (0.0) | 2 (1.3) | 24 (13.8) | 12 (8.8) | 7 (15.2) | 2 (5.0) | 0 (0.0) |
| Remission, n (%)# | 9 (1.3) | 2 (3.2) | 0 (0.0) | 1 (0.6) | 4 (2.3) | 1 (0.7) | 1 (2.2) | 0 (0.0) | 0 (0.0) |
| Other reason, n (%)# | 29 (4.2) | 2 (3.2) | 3 (15.8) | 9 (5.7) | 5 (2.9) | 3 (2.2) | 3 (6.5) | 3 (7.5) | 1 (1.7) |
| Not specified, n (%)# | 3 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.6) | 2 (1.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Lost to follow-up, n (%)# | 21 (3.0) | 3 (4.8) | 0 (0.0) | 5 (3.2) | 3 (1.7) | 5 (3.6) | 3 (6.5) | 1 (2.5) | 1 (1.7) |

#Due to the possibility of multiple answers, the total number of reasons given for treatment discontinuation exceeds the number of terminated treatment courses.

*Abbr.:* ACI, acitretin; ADA, adalimumab; CyA, cyclosporine A; ETA, etanercept; FAE, fumaric acid esters; INF, infliximab; MTX, methotrexate; UST, ustekinumab.

Tobias Arlond et al, Drug survival rates and reasons for drug discontinuation in psoriasis, JDDG, 1610-0379/2016/1411

Τι συμβαίνει όμως με το Secukinumab;

ORIGINAL ARTICLE

# Secukinumab long-term safety experience: A pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis

Peter C. M. van de Kerkhof, MD, PhD,[a] Christopher E. M. Griffiths, MD,[b] Kristian Reich, MD, PhD,[c] Craig L. Leonardi, MD,[d] Andrew Blauvelt, MD, MBA,[e] Tsen-Fang Tsai, MD,[f] Yankun Gong, PhD,[g] Jiaqing Huang, MD, PhD,[h] Charis Papavassilis, MD, PhD,[i] and Todd Fox, RPh, PharmB, ACPR[i]

*Nijmegen, The Netherlands; Manchester, United Kingdom; Göttingen, Germany; Saint Louis, Missouri; Portland, Oregon; Bethesda, Maryland; Taipei, Taiwan; Shanghai, China; East Hanover, New Jersey; and Basel, Switzerland*

Regimen-finding | Regimen-finding | Dose-ranging | Dose-ranging

EXPERT OPINION ON DRUG SAFETY, 2016
http://dx.doi.org/10.1080/14740338.2016.1221923

Taylor & Francis
Taylor & Francis Group

DRUG SAFETY EVALUATION

## Safety of secukinumab in the treatment of psoriasis

Andrew Blauvelt

Oregon Medical Research Center, Portland, OR, USA

1. P. van de Kerkhof, J Am Acad Dermatol. 2016 Jul;75(1):83-98.e4. doi:10.1016/j.jaad.2016.03.024. Epub 2016 May 12
2. Andrew Blauvelt (2016): Safety of secukinumab in the treatment of psoriasis, Expert Opinion on Drug Safety, DOI: 10.1080/14740338.2016.1221923

# 3430 ασθενείς έλαβαν Secukinumab σε 10 μελέτες φάσης 2 και 3 στην ψωρίαση

**Ευνοϊκό προφίλ ασφάλειας, με βάση τον μεγάλο αριθμό κλινικών δεδομένων**

- ✓ **Συχνότερες οι λοιμώξεις ανώτερου αναπνευστικού ήπιας βαρύτητας[1]**
- ✓ **Ήπιες βλεννογοδερματικές καντιντιάσεις που δεν οδηγούν σε διακοπή της αγωγής[1]**
- ✓ **Δεν παρατηρήθηκε ενεργοποίηση προϋπάρχουσας ή λανθάνουσας φυματίωσης στο κλινικό πρόγραμμα της ψωρίασης[2].**
- ✓ **Παρόμοια χαμηλά ποσοστά εμφάνισης σοβαρών λοιμώξεων, κακοηθειών και MACEs με την ομάδα του Etanercept[1]**
- ✓ **Χαμηλή ανοσογονικότητα[3] (0,4 %)**

1. P. van de Kerkhof, J Am Acad Dermatol. 2016 Jul;75(1):83-98.e4. doi:10.1016/j.jaad.2016.03.024. Epub 2016 May 12
2. Andrew Blauvelt (2016): Safety of secukinumab in the treatment of psoriasis, Expert Opinion on Drug Safety, DOI: 10.1080/14740338.2016.1221923, 3. Reich K, et al. AAD 2015, San Francisco, CA (P1320)

# Secukinumab Demonstrates Sustained

## High Efficacy and a Favorable Safety Profile in Moderate to Severe Psoriasis Patients Through 4 Years of Treatment

R. Bissonnette et al, Secukinumab Demonstrates Sustained High Efficacy and a Favorable Safety Profile in Moderate to Severe Psoriasis Patients Through 4 Years of Treatment Presented at 25th European Academy of Dermatology and Venereology Congress, 28 September-2 October, 2016, Vienna, Austria (Oral presentation)

# Σχεδιασμός μελέτης:
# 4 Χρόνια σε θεραπεία με secukinumab


**Οι λόγοι διακοπής της θεραπείας των ασθενών από τη μελέτη στην ομάδα των 300 mg FI (n, %) ήταν:**

- Απόφαση του ασθενούς (10, 6.0%),
- Ανεπιθύμητο συμβάν (9, 5.4%), και
- Έλλειψη αποτελεσματικότητας (7, 4.2%)

Double - blind

Open-label
(home administration)

**99.5% treatment compliance**

BL, baseline; PASI 75, ≥75% improvement in Baseline Psoriasis Area and Severity Index score.
[a]Subjects were treated with secukinumab at Week 12 and then at the start of relapse every 4 weeks until they achieved PASI 75 response again.

R. Bissonnette et al, Secukinumab Demonstrates Sustained High Efficacy and a Favorable Safety Profile in Moderate to Severe Psoriasis Patients Through 4 Years of Treatment Presented at 25th European Academy of Dermatology and Venereology Congress, 28 September-2 October, 2016, Vienna, Austria (Oral presentation)

# Το προφίλ ασφάλειας δεν διαφοροποιείται σε βάθος χρόνου (δεδομένα από 4 έτη)

| Treatment emergent AEs | Year 1 n = 168 n (%) | Year 2 n = 168 n (%) | Year 3 n = 157 n (%) | Year 4 n = 142 n (%) |
|---|---|---|---|---|
| **All AEs** | 131 (78.0) | 126 (75.0) | 109 (69.4) | 88 (62.0) |
| **All SAEs** | 14 (8.3) | 11 (6.5) | 13 (8.3) | 12 (8.5) |
| **Frequent AEs** | | | | |
| Nasopharyngitis | 30 (17.9) | 27 (16.1) | 25 (15.9) | 17 (12.0) |
| Upper respiratory tract infection | 12 (7.1) | 11 (6.5) | 5 (3.2) | 5 (3.5) |
| Headache | 10 (6.0) | 7 (4.2) | 4 (2.5) | 3 (2.1) |
| Pharyngitis | 11 (6.5) | 2 (1.2) | 3 (1.9) | 4 (2.8) |

AE, adverse event; SAE, serious adverse event

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# Το προφίλ ασφάλειας δεν διαφοροποιείται σε βάθος χρόνου (δεδομένα από 4 έτη)

| Treatment emergent AEs | Year 1 n = 168 n (%) | Year 2 n = 168 n (%) | Year 3 n = 157 n (%) | Year 4 n = 142 n (%) |
|---|---|---|---|---|
| **Selected rare AEs** | | | | |
| Opportunistic infections (other than TB and candidiasis) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Tuberculosis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| *Candida* infections | | | | |
| - Vulvovaginal candidiasis | 3 (1.8) | 3 (1.8) | 1 (0.6) | 0 (0.0) |
| - Oral candidiasis | 0 (0.0) | 1 (0.6) | 0 (0.0) | 1 (0.7) |
| Neutropenia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| MACE | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Crohn's Disease | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Ulcerative colitis | 0 (0.0) | 2 (1.2)[1] | 1 (0.6) | 0 (0.0) |
| Malignant or unspecified tumors (excl. NMSC) | 0 (0.0) | 2 (1.2)[2] | 0 (0.0) | 0 (0.0) |

[1]1 case was an exacerbation of previously existing ulcerative colitis; [2]1 case of cholangiocarcinoma, 1 case of invasive ductal breast carcinoma
AE, adverse event; TB, tuberculosis; NMSC, non melanoma skin cancer

[1] + ιστορικό ελκώδους κολίτιδας [2] 1 χολαγγειοκαρκίνωμα & 1 Ca μαστού

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# Secukinumab vs Etanercept: Παρόμοιο προφίλ ασφάλειας με το etanercept

| Variable | Induction Period | | | | Entire Study Period† | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Placebo (N=327) |
| Exposure to study trea | | | | | | | | 95.3±61.0 |
| | | | | | | | | tient-yr) |
| Any adverse event | | | | | | | | 168 (329.7) |
| Death | | | | | | | | 0 |
| Nonfatal serious adver | | | | | | | | 7 (8.3) |
| Discontinuation due to event‡ | | | | | | | | 3 |
| Infection or infestation | | | | | | | | 65 (89.5) |
| Common adverse ever | | | | | | | | |
| Nasopharyngitis | | | | | | | | 26 (32.8) |
| Headache | | | | | | | | 24 (29.6) |
| Diarrhea | | | | | | | | 7 (8.4) |
| Pruritus | | | | | | | | 11 (13.2) |
| Arthralgia | | | | | | | | 10 (12.1) |
| Upper respiratory t | | | | | | | | 3 (3.5) |
| Back pain | | | | | | | | 6 (7.1) |
| Cough | | | | | | | | 4 (4.8) |
| Hypertension | 5 (1.5) | 10 (3.1) | 5 (1.5) | 4 (1.2) | 20 (5.0) | 22 (5.6) | 14 (4.9) | 4 (4.7) |
| Nausea | 8 (2.5) | 6 (1.8) | 4 (1.2) | 7 (2.1) | 11 (2.7) | 10 (2.5) | 7 (2.4) | 7 (8.3) |
| Oropharyngeal pain | 9 (2.8) | 5 (1.5) | 4 (1.2) | 7 (2.1) | 25 (6.3) | 20 (5.0) | 10 (3.5) | 7 (8.3) |

- Το προφίλ ασφάλειας του Secukinumab στα **150 & 300 mg είναι παρόμοιο**. [1]
- Δεν υπήρξε κάποια διαφοροποίηση στο προφίλ ασφάλειας στην περίοδο της δόσης έναρξης (0-12 εβδομάδες) σε σχέση με την καθόλη διάρκεια της θεραπείας των 52 εβδομάδων (0-52 εβδομάδες).[1]
- **Συγκρίσιμο προφίλ ασφάλειας με το Etanercept**, όπως προέκυψε από την συγκριτική μελέτη των 52 εβδομάδων.[1]

Langley RG, et al. N Engl J Med. 2014;371:326–38.

# Secukinumab vs Ustekinumab:
# Παρόμοιο προφίλ ασφάλειας με το ustekinumab

**Table II.** Adverse events during the 52-week study period (exposure-adjusted*)

| | Secukinumab 300 mg n = 335 n (IR) [95% CI] | Ustekinumab n = 336 n (IR) [95% CI] |
|---|---|---|
| Any AE | 286 (280.9) [249.3-315.4] | 278 (250.1) [221.6-281.3] |
| Serious AEs | 30 (9.6) [6.5-13.7] | 26 (8.5) [5.5-12.4] |
| Death | 0 | 1 |
| Discontinued treatment due to AE | 10 | 9 |
| System organ class | | |
| Infections and infestations† | 197 (98.4) [85.1-113.1] | 194 (95.8) [82.8-110.3] |
| Most frequent individual AEs‡ | | |
| Nasopharyngitis | 77 (27.1) [21.4-33.8] | 83 (31.0) [24.7-38.5] |
| Headache | 40 (13.5) [9.7-18.4] | 41 (14.2) [10.2-19.3] |
| Upper respiratory tract infection | 31 (10.1) [6.9-14.3] | 30 (9.9) [6.7-14.2] |
| Arthralgia | 25 (8.1) [5.3-12.0] | 28 (9.2) [6.1-13.3] |
| Diarrhea | 23 (7.5) [4.7-11.2] | 24 (7.9) [5.1-11.8] |
| Back pain | 22 (7.1) [4.4-10.7] | 26 (8.5) [5.6-12.5] |

1. D. Thaci et all, J. Am. Acad. of Dermatology 2015, 2. A Blauvelt et al, J Am Acad Dermatol. 2016 Sep 20. pii: S0190-9622(16)30624-7.doi:10.1016/j.jaad.2016.08.008

Άρα…μπορεί τελικά να συνδυαστεί η μακροχρόνια αποτελεσματικότητα με την ασφάλεια;;;;;;;

? Κλασσικές συστηματικές θεραπείες

✓ Βιολογικές θεραπείες

✓ secukinumab